DISCUSSION OF THE AMENDMENT

The claims have been amended by deleting the solvate embodiment, by changing the "use" claims to corresponding method claims, and replacing "medicament" with --pharmaceutical composition--. Claims 19, 22, 25-28, 32-35, 37-42, 44, 47, 50, 53-56, 60-63, 65-70 and 72 have been canceled.

The claims have been further amended, where applicable, by deleting "preferably"-type language, and improper multiple dependency. New Claims 74-104 have been added to claim the subject matter deleted by this amendment.

No new matter is believed to have been added by the above amendment. Claims 1-18, 20-21, 23-24, 29-31, 36, 43, 45-46, 48-49, 51-52, 57-59, 64, 71 and 73-104 are now pending in the application.

REMARKS

The rejection of Claims 1-7 under 35 U.S.C. § 102(b) as anticipated by Laconde et al, "New Analogues of the Anticancer E7070: Synthesis and Pharmacology," *Journal of Enzyme Inhibition and Medicinal Chemistry*, 2003, vol. 18 (2) pp. 89-94 (Laconde et al), is respectfully traversed. The Examiner relies on one of the particular compounds therein, i.e., benzoic acid, 2-[[[1-](3,4,5-trimethoxyphenyl)methyl]-1H-indol-6-yl]amino]sulfonyl]-, methyl ester.

In reply, this compound of Laconde et al does not anticipate the presently-claimed invention. In the Laconde et al compound, the 3,4,5-trimethoxyphenyl moiety is analogous to the presently-recited R^1 group. However, in Claim 1, R^1 represents a $-NR^8R^9$ radical or, in effect, an optionally substituted cycloaliphatic radical, which may be condensed with an optionally substituted mono- or bicyclic cycloaliphatic ring system. Thus, presently-recited R^1 is not inclusive of phenyl *per se*, or any substituted phenyl group. Accordingly, it is respectfully requested that this rejection be withdrawn.

The rejections of Claims 20-45 and 48-73 under 35 U.S.C. § 101 and under 35 U.S.C. § 112, second paragraph, are respectfully traversed. The so-called "use" claims are now method claims. Accordingly, it is respectfully requested that this rejection be withdrawn.

The rejection of Claims 18-19 and 46-47 under 35 U.S.C. § 112, second paragraph, in the recital of the term "medicament" is respectfully traversed. Indeed, the rejection is now moot in view of the above-discussed amendment. Accordingly, it is respectfully requested that the rejection be withdrawn.

The rejection of Claims 1-17 under 35 U.S.C. § 112, first paragraph, as not enabling for making solvates and hydrates, is respectfully traversed. Indeed, the rejection is now moot in view of the above-discussed amendment. Accordingly, it is respectfully requested that the rejection be withdrawn.

The rejection of Claims 18-73 under 35 U.S.C. § 112, first paragraph, as insufficiently enabling with regard to preventing diseases, is respectfully traversed. According to the Examiner, the prevention of disease would require the skilled clinician to identify individuals who have the potential of developing such diseases, with vaccines being the only established prophylactics.

In reply, prophylaxis refers to any medical or public health procedure to prevent a disease. For example, according to Dictionary of Biochemistry and Molecular Biology, Oxford University Press, 2nd Edition, 2002 (Dictionary), page 707 (**submitted herewith**), prophylaxis is "Measure(s) taken to prevent the occurrence of disease".

Vaccines are just one example of them, since they produce active immunity to prevent an infection; they are administered to healthy individuals, or in some cases, to people suspected to have been exposed to the pathogens but that have not developed the illness. Dictionary defines vaccines as "Any antigenic preparation administered in order to stimulate the recipient's protective immunity to one or more particular pathogens and/or toxins."

Other devices and substances can be administered or used as prophylactics as for instance, the use of antibiotic ointments on burns, or wounds to avoid infection. Antibiotic ointments do not produce active immunity and omission of their application may not trigger any such infection. In fact, their application may prove unnecessary, yet it may still be performed as a precautionary measure.

The compounds of the invention can be used both, by healthy or predisposed individuals to prevent the diseases described and claimed, since they act on the common receptor (receptor 5-HT_6) involved. This would not necessarily require a clinician to predict a future disorder, but instead could be used as a preventive measure to avoid development of said disorders. Thus, once the inhibitory activity of the claimed compounds on the 5-HT_6

receptor has been established, the skilled person would equally consider their activity on the claimed diseases.

Accordingly, it is respectfully requested that the rejection be withdrawn.

The rejection of Claims 18-73 under 35 U.S.C. § 112, first paragraph, as failing to comply with the enablement requirement with regard to disorders or disease relating to food intake, is respectfully traversed. The Examiner applies the so-called *Wands* factors. However, none of the now-claimed methods are considered to be speculative in the prior art, and it is respectfully submitted that one of ordinary skill in the art would be able to practice the method claims, which are all drawn to treatment and/or prophylaxis, by routine experimentation, for reasons discussed above regarding "prevention". In addition, the specification, in the Table and the discussion thereof at page 65, discloses the affinity for the 5-HT_6 receptor of some sample compounds of the invention through values of inhibition constants. The role of the 5-HT_6 receptor in the ingestion of food has been disclosed in the prior art, as acknowledged at page 2, lines 27-28 of the specification. It is therefore reasonable to suggest that the skilled person would be guided into testing the activity of the compounds of the invention on eating disorders, since they exert an inhibitory activity on the 5-HT_6 receptor.

In further support of the above-discussed role of the 5-HT_6 receptor in the treatment of disorders related to food intake, **submitted herewith** (with the IDS, alluded to below) are copies of two papers and two abstracts published before the priority date herein, now discussed:

- Bentley et al, 5-HT6 antisense oligonucleotide i.c.v. affects rat performance in the water maze and feeding. *J. Psychopharmacol.* **1997** *11*, A64-255

This abstract summarizes preliminary findings on the influence that the 5-HT_6 receptor may have in feeding patterns and body weight in rats. In particular, it was found that administration of an antisense oligonucleotide to rats resulted in both, a lower body weight

and food intake compared to mismatch or scrambled oligonucleotides, thus indicating that the effect is sequence specific.

- Woolley et al, A role for 5-HT6 receptors in retention of spatial learning in the Morris water maze. *Neuropharmacology* **2001** *41*, 210-219

This document, described in the specification, further provides results and data supporting the results discussed above. It correlates the administration of a 5-HT_6 antisense oligonucleotide (OA) and a selective 5-HT_6 antagonist Ro 04-6790 with reduced body weight, the first one also being related to a decrease in food consumption. Both compounds have affinity for the receptor, with Ro 04-6790 being an antagonist.

The tests developed and used in the research paper are fully described under the headings "*2.4.3 Food consumption and body weight*" (pages 212-213) and 3.4 "*Food consumption and body weight*" (page 215) in which the results obtained with the different oligodeoxynucleotides (ODNs) are compared (see also Figure 5). Said results manifest that the reduction in food consumption and body weight is exerted and maintained by 5-HT_6 ligands such as AO or Ro 04-6790 and by comparison with control mismatch (MO) and scrambled (SO) oligodeoxynucleotides, the document further proves that the activity is sequence specific. This is further asserted in page 217, last paragraph: "*During the course of the present ODN experiment, only animals receiving 5-HT_6 directed AO, and not MO or SO treatment showed a decrease in both food consumption and body weight suggesting that this receptor may also regulate feeding. This data is in contrast with the studies of Yoshioka et al. (1998) and Hamon et al. (1999), in which treatment with the 5-HT_6 directed AO did not alter body weight [...] In summary, this study identifies a role for 5-HT_6 receptors [...] and in addition suggests it may be involved in modulating feeding.*"

Thus, the reference document implies that the 5-HT_6 receptor regulates food intake and furthermore, that compounds binding to the receptor result in reduced food intake and body weight.

The application of the compounds of the invention in the prophylaxis/treatment of disorders/diseases related to food intake is therefore fully supported: data is provided about the affinity of the compounds for the receptor 5-HT_6, as well as a behavioural model to measure food ingestion.

- Bentley et al, Investigation of stretching behaviour induced by the selective 5-HT6 receptor antagonist Ro 04-6790 in rats. *Br. J. Pharmacol.* **1999** *126*, 1537-1542

This document examines the effects on the Central Nervous System following administration of Ro 04-6790 and does not provide data related to disorder or disease related to food intake. However, it provides the pK_i value for this antagonist, having a binding constant $K_i = 10^{-7.3}$ which is comparable to those reported in the specification herein in the Table at page 65 for some sample compounds. Therefore, these compounds have similar affinity for the receptor.

- Svartengren et al, The serotonin 5-HT6 receptor antagonist BVT.5182 reduces body weight of high fat diet-induced mice, *Int. J. Obes.* **2003** *27, Suppl.l.* Abst T1: P1-094

This abstract manifests that long term decrease in body weight and cumulative food intake are observed when a 5-HT_6 receptor antagonist (BVT.5182) is administered to control and DIO rats, and are similar to those observed after administration of a clinically established anti-obesity drug, sibutramine: "*Repeated treatment with BVT.5182 reduced body weight by 9% and cumulative food intake by 11% in DIO mice (3 mg/kg sc). Sibutramine (10 mg/kg sc) decreased body weight with similar efficacy). BVT.5182 decreased serum leptin as well as epididymal fat.*"

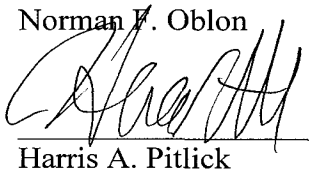
For all the above reasons, it is respectfully requested that this rejection be withdrawn.

Applicants respectfully call the Examiner's attention to the Information Disclosure Statement (IDS) **submitted herewith**. The Examiner is respectfully requested to initial the Form PTO 1449 submitted therewith, and include a copy thereof with the next Office communication.

All of the presently-pending claims in this application are now believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to pass this application to issue.

Respectfully submitted,

OBLON, SPIVAK, McCLELLAND,
MAIER & NEUSTADT, P.C.
Norman F. Oblon



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